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MAR 20 1990
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HIV-1 and hepatitis B transmission in Sudan

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A seroepidemiologic survey was conducted among 773 male soldiers living in five urban locations in Sudan to study the prevalence of and risk factors for HIV-1 and hepatitis B transmission. Twenty-eight per cent of the study population were born and raised in southern Sudan, an area bordering Kenya, Zaire and Uganda, whilst 72% of the study subjects were from northern Sudan. Seventy-eight per cent of the study population had serologic evidence of past hepatitis B infection, and 13 soldiers were confirmed positive for HIV-1 antibody. All 13 HIV-positive soldiers had recently been deployed in southern Sudan. Multivariate analysis indicated an association between living in southern Sudan and both hepatitis B (odds ratio 8.2) and HIV-1 infection (odds ratio 14). Additionally, sexual relations with prostitutes (odds ratio 1.5) and medical injections for schistosomiasis (odds ratio 2.72) were independent predictors of hepatitis B markers in this military population. The findings of this study suggest that sexual promiscuity is a risk factor for hepatitis B transmission in Sudan. They also indicate one possible route for the spread of HIV-1 from central to northern Africa.

AIDS 1989; 3:725-729

Keywords: HIV, hepatitis B, sexually transmitted disease.

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A-1 20

Introduction

Hepatitis B infection is endemic in the developing countries of northeast Africa. In contrast, the prevalence of HIV, which shares many epidemiologic characteristics with hepatitis B [1-3], is reported to be low [4-7]. While the re-use of disposable needles and syringes for medical injections and prostitution have been implicated in the transmission of hepatitis B in this region [7-9], the mechanisms of viral transmission are still poorly understood. A more complete understanding of the epidemiology of hepatitis B is needed to prevent the morbidity associated with this infection, as well as to prevent the spread of HIV infection. The objective of this study was to describe the patterns of HIV-1 and hepatitis B infection among groups of male soldiers living in different regions of Sudan.

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Sponsorship: This research was supported by the US Naval Medical Research and Development Command, NNMCR, Bethesda, MD. Work Unit No. 3M463105H29.AA 335. The opinions and assertions contained

Subjects and methods

Between March 1987 and April 1988, male Sudanese soldiers stationed in the cities of Port Sudan, Kassala, Gederef, Omdurman and Juba were invited to participate in a seroepidemiologic study (Fig. 1). Juba is the largest city in southern Sudan, an area bordering Kenya, Uganda and Zaire. The four other cities are located in the predominantly Muslim provinces of northern Sudan. The north and the south of Sudan are distinct regions, both culturally and religiously. Southern Sudan is currently an area of political upheaval and military conflict. Soldiers from the north are frequently deployed in southern Sudan, and vice versa.

There was a large military population and a military medical care facility in each study site. Enlisted male soldiers presenting to outpatient clinics at these facilities were

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Date of receipt: 17 July 1989.

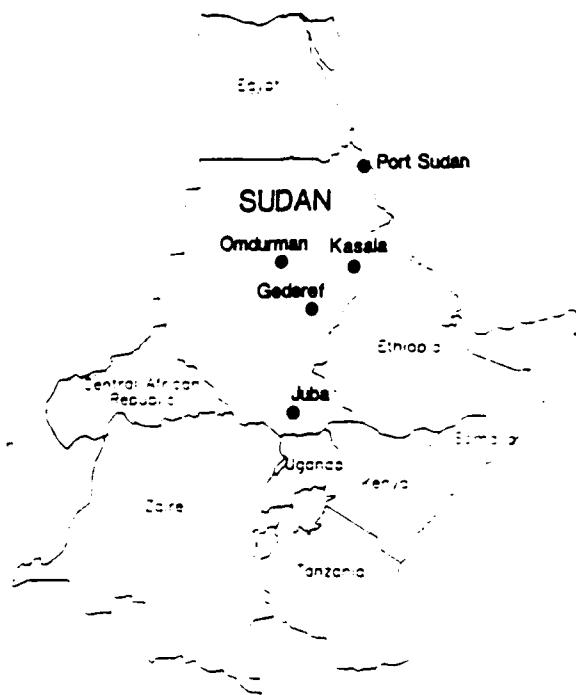


Fig. 1. Study site locations in Sudan.

enrolled into the study on the basis of presentation during the time when the study site was visited. Voluntary, informed consent was obtained from all subjects, and US Navy guidelines for human experimentation and the protection of human subjects were followed. Few eligible soldiers refused to participate in the study. No attempt was made to screen subjects prior to their inclusion in the study.

An epidemiologic questionnaire was completed for all study subjects by a trained Sudanese physician. Basic demographic data, including place of birth and upbringing, and the region where stationed during the previous 5 years were requested from all subjects. Soldiers reporting one of the three southern provinces as their place of birth and upbringing were considered southerners, while all other soldiers were considered northerners. Subjects were also questioned about exposure to potential risk factors for hepatitis B and HIV-1 transmission, including a history of sexual relations with prostitutes and a previous sexually transmitted disease (STD).

A 10 ml sample of venous blood was collected by venipuncture from each study participant. Sera were analysed for the presence of serologic markers to HIV-1 and hepatitis B using commercially available enzyme-linked immunosorbent assay (ELISA) kits (Abbott Laboratories, North Chicago, Illinois, USA). Sera repeatedly reactive by ELISA for antibody to HIV-1 were confirmed positive by Western blot (Dupont, Wilmington, Delaware, USA). All sera were also screened for the presence of hepatitis B surface antigen (HBsAg). Antigen-negative sera were subsequently tested for the presence of hepatitis B surface antibody (anti-HBs) and hepatitis B core antibody (anti-HBc). Sera positive for HBsAg were tested for the presence of hepatitis B e antigen (HBeAg) and antibody to Delta virus (anti-HD).

Information obtained from epidemiologic questionnaires was compared with serologic test results using the chi-square test with Yates' correction, Fisher's exact test and two-tailed Student's *t*-test. Stepwise multiple logistic regression analysis was employed using the SAS computer package (Cary, North Carolina, USA). For statistical analysis of hepatitis B markers, subjects were compared as antigen positive (positive for HBsAg), seropositive [positive for any hepatitis B marker (HBsAg, anti-HBs, or anti-HBc)], and, seronegative (negative for all hepatitis B markers). Means were reported as ± 1 s.d. Significance was determined at the 0.05 level.

Results

Study population

A total of 773 male soldiers participated in the study (mean age 25.8 ± 6.5 years; range, 17–58 years). Twenty-eight per cent (217/773) of study subjects were from the southern provinces, and 72% (556/773) reported one of the northern provinces as their place of birth and upbringing. The mean age of study subjects from the south (25.2 ± 6.4 years) was comparable to the mean age of study subjects from the north (26 ± 6.5 years).

Soldiers raised in the south tended to be less well educated than soldiers from the north (6.4 ± 4.3 versus 8.2 ± 4.0 years of education; $P < 0.001$). Southern soldiers also more often reported a history of ritual scarification, tattooing and an STD (Table 1). Exposure to other potential risk factors for hepatitis B and HIV transmission, including previous parenteral therapy and blood transfusions, were comparable between the two groups. A prior episode of jaundice was also not reported more frequently by either group (Table 1).

Table 1. Comparison of potential risk factors for hepatitis B and HIV-1 transmission between northern and southern soldiers*.

	Northern soldiers		Southern soldiers	
	%	n	%	n
History of				
Scarification	13	73/546	26	54/206†
Tattoo	19	104/541	31	64/209†
Transfusion	1	8/553	1	2/216
Hospitalization	37	203/556	37	81/217
Jaundice	35	190/551	35	75/215
Sex with prostitutes	50	275/555	57	123/216
STD	28	152/549	38	83/217‡
Parenteral therapy for				
Malaria	27	148/555	23	49/215
Schistosomiasis	12	64/554	8	17/217

*Denominator data vary with the number of responses obtained from study subjects. † $P < 0.001$; ‡ $P < 0.01$. STD, sexually transmitted diseases.

Hepatitis B

Twenty-five per cent (197/773) of the entire study population was found to be antigen positive, and anti-HBs or

anti-HBc was detected in an additional 409 study subjects. Seventy-eight per cent of soldiers were, therefore, seropositive for at least one hepatitis B marker. Of HBsAg-positive samples with sufficient volumes of sera available for further testing, 8% (16/195) were positive for HBeAg and 10% (16/166) were positive for anti-HD.

The prevalence of seropositivity for hepatitis B was significantly higher among soldiers from the south (95%) when compared with soldiers from the north (72%; Table 2). The prevalence of HBsAg was also higher among southerners (28 versus 25%), but this difference was not statistically significant. There was no significant difference in the prevalence of HBeAg and anti-HD between soldiers from the north and the south.

Table 2. Comparison of the prevalence of serologic markers for HIV-1 and hepatitis B between soldiers born in the north and south of Sudan.

	North		South	
	%	n	%	n
HIV-1	0	2/556	5	11/217*
HBsAg	25	137/556	28	60/217
Seropositive (HBsAg, anti-HBs, or anti-HBc)	72	400/556	95	206/217*
HBeAg	7	10/135	10	6/60
Anti-HD	10	11/114	10	5/52

* $P < 0.001$. HBsAg, hepatitis B surface antigen; anti-HBs, hepatitis B surface antibody; anti-HBc, hepatitis B core antibody; HBeAg, hepatitis B e antigen; anti-HD, antibody to Delta virus.

Age-specific analysis of hepatitis B markers revealed that the pattern of hepatitis B transmission differed between individuals from the north and those born and raised in the south. In the north, the prevalence of seropositivity showed an increasing pattern of infection from 47.5%, in subjects less than 20 years of age, to more than 80% in subjects over age 39. Similarly, the prevalence of HBsAg was noted to increase with age among subjects raised in the north (Fig. 2). In contrast, hepatitis B infection was not found to increase after the age of 20 among soldiers raised in the south because nearly all soldiers (94%) under 20 years of age had serologic evidence of hepatitis B infection. Also, antigenemia was highest in the younger age groups in the south (Fig. 2).

Fifty per cent of soldiers raised in the north admitted to prior sexual relations with prostitutes compared with 57% raised in the south. Among soldiers raised in the north, the prevalence of hepatitis B markers was increased in individuals with a history of sexual relations with prostitutes when compared to soldiers denying such activity (Fig. 3). A comparable pattern of hepatitis B transmission was not found among soldiers raised in the south; however, nearly all subjects in this population had been infected with hepatitis B prior to age 20 (Fig. 2).

Multivariate analysis was performed to determine independent associations between serologic markers and potential risk factors of hepatitis B infection. Risk factors independently predictive of seropositivity for any hepatitis B

marker were birth and upbringing in the south, sexual relations with prostitutes, a history of parenteral therapy for schistosomiasis and age (Table 3). Potential risk factors that were not associated with HBsAg-positivity or seropositivity in this study population included a history of blood transfusions, jaundice, ritual scarification, tattooing, and a prior STD. HBeAg and anti-HD were not related to any potential risk factors for hepatitis transmission.

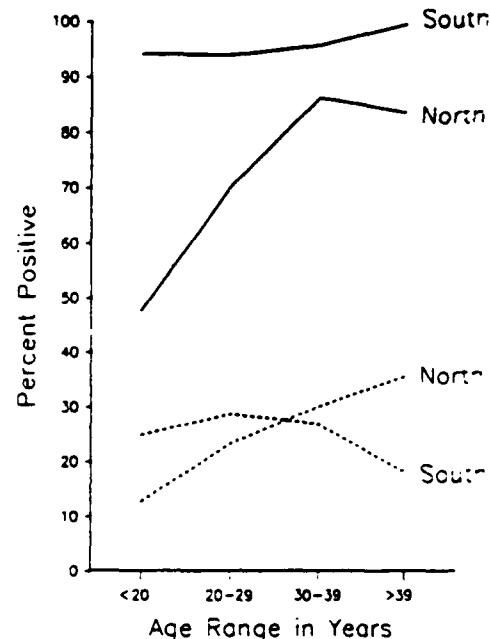


Fig. 2. Comparison of the age-specific prevalence of hepatitis B markers between northern ($n = 556$) and southern ($n = 217$) soldiers. — seropositivity; --- HBsAg positivity.

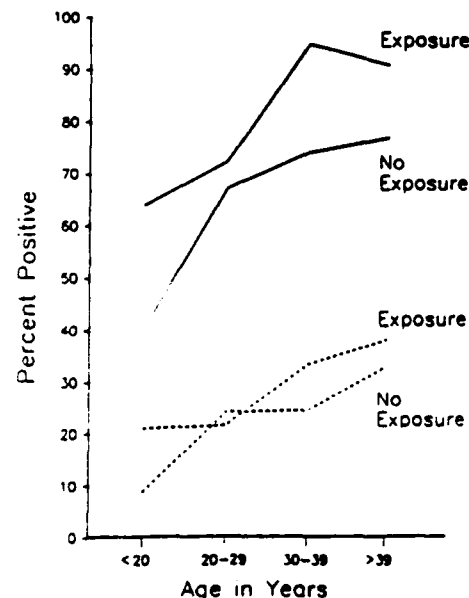


Fig. 3. Comparison of serologic markers for hepatitis B between northern soldiers with a history of exposure to prostitutes ($n = 269$) and northern soldiers denying past sexual exposure to prostitutes ($n = 276$). — seropositivity; --- HBsAg positivity.

Table 3. Multivariate analysis of hepatitis B markers and HIV antibody and risk factors of infection

Variable	Beta coefficient	Odds ratio	95% confidence interval	P value
Seropositive (HBsAg, anti-HBs or anti-HBc)				
Born/raised in the south	2.10	8.20	4.24-16.6	<0.001
Sex with prostitutes	0.40	1.50	1.02-2.17	0.04
Parenteral therapy for schistosomiasis†	1.0	2.70	1.25-5.93	0.01
Age (per year)	0.06	1.06	1.03-1.10	<0.001
HIV-1 positive*				
Born/raised in the south	2.65	14.00	2.72-73.60	0.001
Education (per year)	-0.14	1.15	1.00-2.90	0.05
Hospitalization†	0.54	1.72	1.15-2.55	0.007

*Thirteen HIV-1-positive study subjects were available for multivariate analysis. †Odds ratios based on each additional course of parenteral therapy for schistosomiasis or each hospitalization.

HIV-1

Thirteen soldiers (1.7%) were confirmed positive for HIV-1 antibody by Western blot. Eleven HIV-positive samples were collected in the southern city of Juba, and two were collected in the northern cities of Gederef and Port Sudan (Table 2). Of the eleven HIV-positive soldiers found in Juba, two were northerners who had been stationed in the south for the previous 5 years. The two HIV-positive soldiers sampled in Gederef and Port Sudan had been recently transferred to northern Sudan from Juba. Hence, all HIV infection was found among soldiers who had been living in southern Sudan during the past 5 years.

Compared with HIV-negative soldiers, HIV-positive soldiers more often gave a history of sexual relations with prostitutes (77 versus 51%) and a history of a prior STD (54 versus 30%). The prevalence of hepatitis B markers was also higher among HIV-positive soldiers (100 versus 78%; Table 4). The mean age of HIV-positive soldiers (25.3 years) was similar to the mean age of HIV-negative soldiers (25.7 years).

Risk factors found by multivariate analysis to be independently predictive of HIV-1 infection were birth and upbringing in the south and the number of prior hospitalizations. Furthermore, the level of education attained by study subjects was inversely predictive of HIV infection (Table 3).

Discussion

An important finding of this study was the absence of HIV-1 infection among soldiers stationed exclusively in north-

ern Sudan, whereas 5% of southerners were confirmed HIV-antibody positive. The increased risk of HIV infection in the south of Sudan is consistent with the proximity of this region to Uganda, Zaire and Kenya, where HIV infection is endemic [10]. This finding suggests that HIV-1 may have been introduced into southern Sudan from neighbouring countries [11-13]. A common history of sexual relations with prostitutes, often from central Africa, and prior STDs among HIV-positive soldiers suggest one possible route of HIV infection in southern Sudan. Sexual transmission would be consistent with the epidemiology of HIV infection in neighbouring African countries [14-16], but a firm conclusion about the route of transmission in this group of soldiers was not possible because only 13 HIV-positive individuals were available for comparison.

Finding no HIV-1 infection among soldiers stationed exclusively in northern Sudan is comparable to the findings of previous studies conducted in this region [6-7]. These findings imply that HIV transmission may be less extensive in northern Sudan. However, HIV infection could be introduced into northern Sudan by individuals who have become infected while living in the south, as was found with two soldiers in this study.

A significantly higher prevalence of hepatitis B infection was also found among soldiers from southern Sudan compared with soldiers born and raised in the northern provinces. In the south, nearly all hepatitis B infection occurred before the age of 20 years, rather than the pattern of increasing infection with advancing age which was noted in northern Sudan. A higher prevalence of hepatitis B infection was found also among northern soldiers admitting to sexual relations with prostitutes. This finding is similar

Table 4. Comparison of potential risk factors of infection in HIV-positive and HIV-negative study subjects

	HIV-1-positive		HIV-1-negative*		P value
	%	n	%	n	
Born in the south	85	11/13	27	206/760†	<0.001
Sex with prostitutes	77	10/13	51	388/758	0.12
History of STD	54	7/13	30	228/753	0.14
HBsAg-positive	46	6/13	25	191/760	0.15
Seropositive (HBsAg, anti-HBs or anti-HBc)	100	13/13	78	593/760**	0.12

*Denominator data vary with the number of responses obtained from study subjects. **Ten serum samples had insufficient volumes to test for all hepatitis B markers. †P < 0.001. STD: sexually transmitted disease; HBsAg, hepatitis B surface antigen; anti-HBs, hepatitis B surface antibody; anti-HBc, hepatitis B core antibody.

to data reported in previous studies conducted in northern Sudan [7], indicating an association between hepatitis B infection and sexual promiscuity in this region. These data also indicate a potential for sexual transmission of HIV infection in the north [15].

The independent association found in this study between hepatitis B markers and a history of parenteral therapy for schistosomiasis is consistent with the findings of other studies conducted in northern Africa [7-9]. Since the re-use of disposable needles and syringes has been reported to be a potential risk factor for HIV infection in neighbouring countries [10,14,16], medical injections could also play a role in HIV transmission in Sudan. However, the association in this study between hospitalization and HIV infection could indicate poorer health of HIV-positive subjects in this population rather than a causal relationship.

The inverse association found between education and HIV positivity is noteworthy. Other studies in Africa have reported the converse: that higher education and/or socioeconomic status is associated with HIV transmission [17,18]. A similar inverse association for hepatitis B, however, has been previously described in Sudan [7]. This inverse association may reflect differences in socioeconomic status within this military population. If the less well-educated soldiers are patronizing more promiscuous prostitutes of lower socioeconomic status, they may be at higher risk for HIV and hepatitis B infection [11].

The findings in this study suggest that sexual promiscuity is a risk factor for hepatitis B transmission in Sudan. These findings also indicate one possible route for the spread of HIV from central to northern Africa.

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